UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/545,162	04/07/2000	ANTHONY P. SHUBER	EXT-026	1013

7590 04/02/2004

Patent Administrator
Testa Hurwitz & Thibeault LLP
Hight Street Tower 125 High Street
Boston, MA 02110

EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 04/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/545,162	SHUBER, ANTHONY P.	
	Examiner	Art Unit	
	Juliet Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is written in response applicant's correspondence submitted 11/12/03. The response filed 111/12/03 included a response to the non-final office action and a 1.132 declaration. Applicant's arguments and declaration have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

2. Claims 7-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for screening a patient for colorectal cancer or precancer by determining in fecal matter a ratio between a first amount of long nucleic acid of a length greater than 200 base pairs and a second amount of nucleic acid of a length less than said long nucleic acid, does not reasonably provide enablement for the detection of other types of cancer or precancer or the use of tissues or body fluids other than fecal matter or methods which do not specify the length of the nucleic acids which are detected. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claimed invention is drawn to encompass the identification of patients having any cancer or precancer by determining, in any body fluid or tissue comprising exfoliated cells, the presence of a fragment of nucleic acid that is "of a greater length than a length of said nucleic acid expected to be present in a sample from a healthy

person" or whether an amount of DNA fragment greater than 200 base pairs exceeds a predetermined amount, wherein the DNA fragment is a degradation product of DNA that is present in both normal and precancerous cells or the ratio of long nucleic acids versus short nucleic acids. The specification demonstrates the method using a fecal matter sample for the screening of a patient for colorectal cancer or precancer by detecting the amount of three different long nucleic acid molecules (p53, K-ras, and apc). The specification demonstrates that for these three molecules PCR products of longer than 200 base pairs were present in the fecal matter of patients with colorectal cancer or precancer but such fragments were not present in healthy patients (Example 1). Neither the specification nor the prior art demonstrate that such a relationship exists for other cancers or for other body fluids or for lengths of less than 200 base pairs (as is encompassed by claim 7). The level of unpredictability for the detection of any disease using a nucleic acid assay is quite high. Since neither the specification nor the prior art provide any evidence of a universal association between a ration of nucleic acids greater than 200 base pairs to nucleic acids shorter than 200 base pairs and every cancer and every body fluid, a practitioner wishing to practice the claimed invention would be required to provide the extensive experimentation necessary to demonstrate such an association. Such experimentation would in itself be inventive.

In light of the lack of guidance in the specification and the prior art, and in light of the high level of unpredictability in the instant subject matter, it is concluded that undue experimentation would be required to practice the instant invention commensurate in scope with the claimed invention.

It is noted that the claims that are present in allowed patent US 6143529 are of very similar scope to the instantly claimed invention. The instant rejection is not intended to call into question the validity of these claims because the claims in the '529 patent were allowed over a declaration.

Double Patenting

3. The double patenting rejections are withdrawn in view of the terminal disclaimers.

Response to Declaration

The Declaration under 37 CFR 1.132 filed November 11, 2003 is insufficient to overcome the rejection of the claims based upon 35 U.S.C. 112, first paragraph as set forth in the last Office action because:

The declaration is significantly an opinion declaration by the inventor, which is given some weight, but which is not sufficient to overcome the prima facie case. The declaration also includes data, but the data does not support the conclusion that the method may be used for any type of cancer. For example, Exhibit D shows that the method completely failed to detect any cancers of the Esophagus, failed to detect a significant number of lung cancers and Exhibit E also shows that many lung cancers were not detected by the method. In fact, no cancers of the Esophagus were apparently found using the method based upon a review of Applicant's own exhibits. This supports the conclusion of the enablement rejection that while the method may be useful for detection of colon cancer, it is not useful for all cancers. Further, the scope of the claim is not limited to cancers of the gastrointestinal tract, some of which like

esophageal cancer are not detected, but includes cancers outside this area, ranging from skin cancer to brain cancer, to cancers of every possible tissue type. Most of these cancers are not connected with the GI tract. The evidence of record, as presented by Applicant, contradicts the conclusion drawn by Applicant. The data presented suggests that the method will not work with every cancer, and in fact does not work with a very significant number of lung cancers and no esophageal cancers, according to Applicant's own data. Therefore, the claims are not commensurate in scope with the enabled embodiments. As MPEP 2164.05 states,

> "To overcome a prima facie case of lack of enablement, applicant must demonstrate by argument and/or evidence that the disclosure, as filed, would have enabled the claimed invention for one skilled in the art at the time of filing. This does not preclude applicant from providing a declaration after the filing date which demonstrates that the claimed invention works. However, the examiner should carefully compare the steps, materials, and conditions used in the experiments of the declaration with those disclosed in the application to make sure that they are commensurate in scope; i.e., that the experiments used the guidance in the specification as filed and what was well known to one of skill in the art. Such a showing also must be commensurate with the scope of the claimed invention, i.e., must bear a reasonable correlation to the scope of the claimed invention."

Here, where Applicant's claims are broadly drawn to any tissue source whatsoever and the data presented does not support this breadth of claim. Further, as noted previously, claim 7 is not limited to any particular nucleic acid length. So this claim is further not enabled because there is no disclosure of which lengths would be normally found in different cancers.

Response to Argument

Applicant's arguments filed November 12, 2003 have been fully considered but they are not persuasive. Applicant, in the arguments, relies upon the declaration. Because the declaration is not persuasive for the reasons given above, none of the arguments are persuasive.

Conclusion

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Switzer whose telephone number is 703 306 5824. The examiner can normally be reached on Monday through Thursday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703 308 1119. The fax phone numbers

for the organization where this application or proceeding is assigned are 703 305 3592 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 0196.

JEFFREY FREDMAN
PRIMARY EXAMINER

Juliet C. Switzer
Patent Examiner
AU 1634

March 18, 2004